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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,169	04/20/2007	Toshiaki Tagawa	701018	1668

23460 7590 07/30/2009

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EXAMINER	
HUFF, SHEELA JITENDRA	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
07/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,169	TAGAWA ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed on 6/8/09 has been considered. Applicant's arguments are deemed to be persuasive-in-part.

The rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of applicant's amendment.

The double patenting rejection is withdrawn in view of applicant's argument.

Election/Restrictions

Newly submitted claims 25-27 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: they are directed to a process of making a liposome which step were not part of the originally examined claims.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 25-27 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7, 11-16 and 20-24 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Modi US 6193997. The rejection is re-written in view of the addition of newly filed claims 22-24.

This reference discloses mixed liposome pharmaceutical formulations comprising a protenic pharmaceutical agent, water, at least one membrane-mimetic amphiphile and at least one phospholipid wherein the phospholipid can be phospholipid GLA (glycolic, lactic acid) and/or triolein (reads on applicant's triglycerol) (see col. 3, lines 30-65). The protenic pharmaceutical agent can be monoclonal and polyclonal antibodies (reads on ligands of claims 12-15), chemotherapeutic agents and other non proteinaceous compounds such as anitsense oligos and RNA (see col. 5, lines 5-20). The size of liposomes are less than 10nm (col. 6, lines 42-44).

The terminology in claim 21 "for diagnosis and/or therapeutic treatment of cancer" is intended use and carries no patentable weight when evaluating a compound claim.

Claims 22-24 are product-by-process claims and when evaluating compound claims the process does not carry any weight.

While the reference is silent as to the encapsulation rate of the compound in the internal cavity, it is inherent that the encapsulation rate of the reference is the same as that of the claimed invention. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed encapsulation rate with that of the reference, the burden of proof is upon the Applicants to show a distinction between the rates. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Response to applicant's arguments

Applicant argues that the mixed liposome of the reference is different from the liposome of the instant invention because the liposome thickness of the instant invention is different from the reference. These limitations are not in the claims. The claims as they currently stand require a particle size of 300nm of less and the reference meets this limitation. Applicant is cautioned against the addition of new matter into the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 9-24 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Modi US 6193997 in view of Slater et al US 2003/0133973. The rejection is re-written in view of the addition of claims 22-24.

Modi has been discussed above.

This reference does not disclose the internal cavity comprising a compound and a polysaccharide, the compounds of claims 9-10, 17 and 18 or the ligand and/or polymer binding to the external surface of the liposome.

Slater et al disclose liposomes which have hydrophilic polymer chains on the outside of liposomes and the polymer can be polyethylene glycol (0064-0067). The reference also discloses agents (inlcuedes compounds of MW 400-2,000,000 daltons and polyanionc polymers entrapped in the liposomes and these include sulfate polysaccharies, hyaluronic acid, chrondotin sulfate, celluloses and cellulose derivatives (0093-0094).

In view of the disclosure of Slater et al which shows that liposomes can also comprise polyethylene glycol, sulfate polysaccharies, hyaluronic acid, chrondotin sulfate, celluloses and cellulose derivatives it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use those compounds in the formation of a liposome. The terminology in claim 21 "for diagnosis and/or therapeutic treatment of cancer" is intended use and carries no patentable weight when evaluating a compound claim. Claims 22-24 are product-by-process claims and when evaluating compound claims the process does not carry any weight.

Response to applicant's arguments

Applicant's arguments have been discussed above.

Applicant also argues unexpected results. There is no objective evidence of record to show that liposomes of the instant invention are more stable than the liposomes of Modi et al.

Claims 1-5, 7-8 and 11-24 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Modi US 6193997 in view of EP 1170018 and applicant's admission

on page 6 of the specification. The rejection is re-written in view of the addition of claims 22-24.

Modi has been discussed above.

This reference does not disclose the compounds of claims 8, 17 and 18 or the ligand and/or polymer binding to the external surface of the liposome.

The EP reference discloses ligand bonded complexes wherein the ligand (such as an antibody directed against a tumor) is bonded thru a water-soluble macromolecule such as polyethylene glycol, polyglycolic acid, polylactic acid, polyvinylpyrrolidone and/or polyalkylene glycol to a liposome wherein the liposome encapsulates an active medicament (col. 2, lines 20-58 and col. 5, lines 25-38). The size of liposomes are about 20-500nm (col. 6, line 10). A variety of different drugs can be encapsulated into the liposome and they include cisplatin and a variety of other anti-tumor agents.

On page 6 of the specification applicant admits that cisplatin, carboplatin, nedaplatin, gemcitabine and Ara-C are anti-tumor agents.

In view of Modi which dislcoses the incorporation of chemotherapetuic agents into the liposomes, and since both applicant and the EP reference disclose cisplatin as such an agent and since applicant admits that cisplatin, carboplatin, nedaplatin, gemcitabine and Ara-C are anti-tumor agents, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to incorporation any of the known anti-tumor agents into the liposomes of Modi with the expected benefit of treating cancer. Furthermore, in view of the EP reference it also would have been obvious to attach the antibody to the outside of the liposome thru a polyethylene glycol with the

added benefit of specifically targeting the tumor. Claims 22-24 are product-by-process claims and when evaluating compound claims the process does not carry any weight.

Response to applicant's arguments

Applicant's arguments have been discussed above.

Applicant also argues unexpected results. There is no objective evidence of record to show that liposomes of the instant invention are more stable than the liposomes of Modi et al.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Monday-Thursday 6am to 2pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sheela J Huff/
Primary Examiner
Art Unit 1643

sjh